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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,443	XIE ET AL.	
	Examiner	Art Unit	
	STEPHANIE K. MUMMERT	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *30,31,35 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/29/05; 2/10/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner of record has changed. Please address all future correspondence to Examiner Mummert, whose contact information is included at the conclusion of this action.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-29 and 32-34 in the reply filed on January 11, 2008 is acknowledged.

Claims 30-31 and 35-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on January 11, 2008.

Claims 1-29 and 32-34 are pending and will be examined.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on February 10, 2005 and July 29, 2005 were filed in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1, 4-7, 11-12, 14-18, 21-24 and 28-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Lopez-Sabater et al. (Letters in Applied Microbiology, 1997, vol. 24, p. 101-104). Lopez-Sabater teaches a method for the magnetic immunoseparation for detection of viral sequences by PCR (Abstract).

With regard to claim 1, Lopez-Sabater teaches a process for amplifying a nucleic acid of a target cell or virus, which process comprises:

a) contacting a sample containing or suspected of containing a target cell or virus with a magnetic microbead (p. 102, 'immunomagnetic separation' heading, where the sample including the oyster extract suspected of containing hepatitis A virus is contacted with a variety of amounts of magnetic particles and incubated for 2 hours);

b) allowing said target cell or virus, if present in said sample, to bind to said magnetic microbead to form a conjugate between said target cell or virus and said magnetic microbead (p. 102, 'immunomagnetic separation' heading, where the sample including the oyster extract suspected of containing hepatitis A virus is contacted with a variety of amounts of magnetic particles and after incubated for 2 hours); and

c) separating said conjugate from other undesirable constituents via a magnetic force to isolate said target cell or virus from said sample (p. 102, 'immunomagnetic separation' heading, where the sample including the oyster extract suspected of containing hepatitis A virus is contacted with a variety of amounts of magnetic particles and incubated for 2 hours, afterwards, beads were pulled aside with a magnetic separator, fluid removed and beads washed); and

d) applying said separated conjugate to a nucleic acid amplification system to amplify a nucleic acid from said target cell or virus (p. 102, 'immunomagnetic separation' heading, where at the

final step, the beads were washed and ready for PCR assay; p. 102, 'RT-PCR assay' heading, where the beads were heated to denature the virus and release the genome, followed by amplification).

With regard to claim 4, Lopez-Sabater teaches an embodiment of claim 1, wherein the target cell is selected from the group consisting of an animal cell, a plant cell, a fungus cell, a bacterium cell, a recombinant cell and a cultured cell (p. 102, col. 1, where American oysters were inoculated with HAV, oyster cells were diced and homogenized and where this is an animal cell).

With regard to claim 5, Lopez-Sabater teaches an embodiment of claim 1, wherein the target virus is an eucaryotic cell virus or a bacteriophage (p. 102, col. 1, where American oysters were inoculated with HAV; HAV is hepatitis A virus, see Abstract, which is a eucaryotic cell virus).

With regard to claim 6, Lopez-Sabater teaches an embodiment of claim I, wherein the magnetic microbead comprises a magnetizable substance selected from the group consisting of a paramagnetic substance, a ferromagnetic substance and a ferrimagentic substance (p. 102, 'magnetic beads and antibodies (coating IMB) heading', where the beads comprise streptavidin MagneSphere™ paramagnetic beads, where these beads comprise a paramagnetic substance).

With regard to claim 7, Lopez-Sabater teaches an embodiment of claim 6, wherein the magnetizable substance comprises a metal composition (p. 102, 'magnetic beads and antibodies (coating IMB) heading', where the beads comprise streptavidin MagneSphere™ paramagnetic beads, where these beads comprise a paramagnetic substance).

With regard to claim 11, Lopez-Sabater teaches an embodiment of claim 1, wherein the magnetic mierobead has a diameter ranging from about 5 to about 50,000 nanometers (p. 102, 'magnetic beads and antibodies (coating IMB) heading', where the beads comprise streptavidin MagneSphere™ paramagnetic beads, where these beads comprise a paramagnetic substance and the beads are 0.5μm diameter).

With regard to claim 12, Lopez-Sabater teaches an embodiment of claim 1, wherein the magnetic microbead is untreated or modified with an organic molecule (p. 102, 'magnetic beads and antibodies (coating IMB) heading', where the beads comprise streptavidin MagneSphere™ paramagnetic beads).

With regard to claim 14, Lopez-Sabater teaches an embodiment of claim 1, wherein the magnetic microbead is modified to comprise a moiety that specifically binds to the target cell or virus (p. 102, 'magnetic beads and antibodies (coating IMB) heading', where the beads comprise streptavidin MagneSphere™ paramagnetic beads coated with biotinylated human anti-HAV IgG, which binds to the target cell or virus).

With regard to claim 15, Lopez-Sabater teaches an embodiment of claim 14, wherein the moiety is an antibody or functional fragment thereof (p. 102, 'magnetic beads and antibodies (coating IMB) heading', where the beads comprise streptavidin MagneSphere™ paramagnetic beads coated with biotinylated human anti-HAV IgG).

With regard to claim 16, Lopez-Sabater teaches an embodiment of claim 1, wherein the target cell or virus, if present in the sample, is allowed to bind to the magnetic microbead nonspecifically or with low specificity to form the conjugate (p. 102, 'immunomagnetic separation' heading, where the sample including the oyster extract suspected of containing

hepatitis A virus is contacted with a variety of amounts of magnetic particles and incubated for 2 hours, afterwards, beads were pulled aside with a magnetic separator, fluid removed and beads washed).

With regard to claim 17, Lopez-Sabater teaches an embodiment of claim 1, wherein the target cell or virus, if present in the sample, is allowed to bind to the magnetic microbead with high specificity to form the conjugate (p. 102, 'immunomagnetic separation' heading, where the sample including the oyster extract suspected of containing hepatitis A virus is contacted with a variety of amounts of magnetic particles and incubated for 2 hours, afterwards, beads were pulled aside with a magnetic separator, fluid removed and beads washed).

With regard to claim 18, Lopez-Sabater teaches an embodiment of claim 1, which further comprises washing the separated conjugate to remove the undesirable constituents before applying separated conjugate to a nucleic acid amplification system (p. 102, 'immunomagnetic separation' heading, where the beads are trapped to the side of the microcentrifuge tube, the supernatant removed and beads washed six times prior to further processing).

With regard to claim 21, Lopez-Sabater teaches an embodiment of claim 1, which is conducted in an eppendorf tube (p. 102, col. 2, where the process is carried out in microcentrifure tubes which are eppendorf tubes).

With regard to claim 22, Lopez-Sabater teaches an embodiment of claim 1, which is conducted in the absence of a precipitation or centrifugation procedure (p. 102, col. 2, 'immunomagnetic separation' heading, where the separation is carried out using a strong magnetic particle separator stand).

With regard to claim 23, Lopez-Sabater teaches an embodiment of claim 1, which is conducted in the absence of a poisonous agent (p. 102, 'immunomagnetic separation' heading, where the sample including the oyster extract suspected of containing hepatitis A virus is contacted with a variety of amounts of magnetic particles and incubated for 2 hours, afterwards, beads were pulled aside with a magnetic separator, fluid removed and beads washed and where no poisonous agent is added).

With regard to claim 24, Lopez-Sabater teaches an embodiment of claim 1, which is conducted at an ambient temperature ranging from about 0°C to about 35°C without temperature control (p. 102, 'immunomagnetic separation' heading, where the incubation of sample with beads is carried out at room temperature).

With regard to claim 28, Lopez-Sabater teaches an embodiment of claim 1, wherein the nucleic acid amplification system is selected from the group consisting ofpolymerase chain reaction (PCR), ligase chain reaction (LCR), nucleic acid sequence-based amplification (NASBA), strand displacement amplification (SDA) and transcription-medicated amplification (TMA) (p. 102, 'immunomagnetic separation' heading, where at the final step, the beads were washed and ready for PCR assay; p. 102, 'RT-PCR assay' heading, where the beads were heated to denature the virus and release the genome, followed by amplification).

With regard to claim 29, Lopez-Sabater teaches an embodiment of claim 1, which further comprises removing cells from a sample containing or suspected of containing a target virus or bacteriophage before contacting the sample with a magnetic microbead (p. 102, col. 1, 'recovery' heading, where the oyster cells were diced and homogenized, therefore the cells were removed before contacting with a magnetic microbead).

2. Claims 1-4, 6-10, 12-15, 17-18, 22-23, 27-28 and 32-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Olsvik et al. (Clinical Microbiology Reviews, 1994, vol. 7, no. 1, p. 43-54). Olsvik teaches an overview of immunomagnetic separation using paramagnetic particles coated with antibodies for isolation of eukaryotic cells (p. 43, col. 1).

With regard to claim 1, Olsvik teaches a process for amplifying a nucleic acid of a target cell or virus, which process comprises:

a) contacting a sample containing or suspected of containing a target cell or virus with a magnetic microbead (p. 43, where immunomagnetic separation comprises using small super-paramagnetic beads coated with antibodies against surface antigens of cells);

b) allowing said target cell or virus, if present in said sample, to bind to said magnetic microbead to form a conjugate between said target cell or virus and said magnetic microbead (p. 43, where immunomagnetic separation comprises using small super-paramagnetic beads coated with antibodies against surface antigens of cells; see Figure 1 and 2); and

c) separating said conjugate from other undesirable constituents via a magnetic force to isolate said target cell or virus from said sample (p. 43, where immunomagnetic separation comprises using small super-paramagnetic beads coated with antibodies against surface antigens of cells; see Figure 1 and 2; p. 43 where the isolated fraction can be washed and then further processed); and

d) applying said separated conjugate to a nucleic acid amplification system to amplify a nucleic acid from said target cell or virus (p. 46, col. 1, where immunomagnetic separation concentrates

bacteria into a suitable volume and removes PCR inhibtors, the cells are opened and the nucleic acid is available for PCR).

With regard to claim 2, Olsvik teaches an embodiment of claim 1, wherein the sample is a clinical sample (Table 2, where a variety of clinical microbiological targets can be detected using immunomagnetic separation; p. 43, where the technique has found several medical applications).

With regard to claim 3, Olsvik teaches an embodiment of claim 1, wherein the sample is selected from the group consisting of serum, plasma, whole blood, sputum, cerebral spinal fluid, amniotic fluid, urine, gastrointestinal contents, hair, saliva, sweat, gum scrapings, marrow, tissue and cell culture (Table 2, where a variety of clinical microbiological targets can be detected using immunomagnetic separation; p. 43, where the technique has found several medical applications including isolation of eukaryotic cells from fluids such as blood).

With regard to claim 4, Olsvik teaches an embodiment of claim 1, wherein the target cell is selected from the group consisting of an animal cell, a plant cell, a fungus cell, a bacterium cell, a recombinant cell and a cultured cell (p. 43, where eukaryotic cells can be isolated from blood, or the technique can be applied to the detection of prokaryotic organisms such as bacteria and viruses).

With regard to claim 6, Olsvik teaches an embodiment of claim 1, wherein the magnetic microbead comprises a magnetizable substance selected from the group consisting of a paramagnetic substance, a ferromagnetic substance and a ferrimagentic substance (p. 43, where the beads are small and super-paramagnetic; p. 44, col. 1-2, where the particles are super paramagnetic, or magnetic in a field but non-magnetic as soon as the field is removed).

With regard to claim 7, Olsvik teaches an embodiment of claim 6, wherein the magnetizable substance comprises a metal composition (p. 44, col. 2, where the particles comprise metal oxides, including iron).

With regard to claim 8, Olsvik teaches an embodiment of claim 7, wherein the metal composition is a transition metal composition or an alloy thereof (p. 44, col. 2, where the particles comprise metal oxides, including iron).

With regard to claim 9, Olsvik teaches an embodiment of claim 8, wherein the transition metal is selected from the group consisting of iron, nickel, copper, cobalt, manganese, tantalum, zirconium and cobalt-tantalum-zirconium (CoTaZr) alloy (p. 44, col. 2, where the particles comprise metal oxides, including iron).

With regard to claim 10, Olsvik teaches an embodiment of claim 7, wherein the metal composition is Fe_3O_4 (p. 44, col. 2, where the particles comprise metal oxides, including iron).

With regard to claim 12, Olsvik teaches an embodiment of claim 1, wherein the magnetic microbead is untreated or modified with an organic molecule (p. 45, Table 1, where magnetic beads can have a variety of organic molecule coatings, including hydroxyl, epoxy and amine groups).

With regard to claim 13, Olsvik teaches an embodiment of claim 1, wherein the magnetic microbead is modified to comprise a hydroxyl, a carboxyl or an epoxy group (p. 45, Table 1, where magnetic beads can have a variety of organic molecule coatings, including hydroxyl, epoxy and amine groups).

With regard to claim 14, Olsvik teaches an embodiment of claim 1, wherein the magnetic microbead is modified to comprise a moiety that specifically binds to the target cell or virus (p.

43, where immunomagnetic separation comprises using small super-paramagnetic beads coated with antibodies against surface antigens of cells; see Figure 1 and 2).

With regard to claim 15, Olsvik teaches an embodiment of claim 14, wherein the moiety is an antibody or functional fragment thereof (p. 43, where immunomagnetic separation comprises using small super-paramagnetic beads coated with antibodies against surface antigens of cells; see Figure 1 and 2).

With regard to claim 17, Olsvik teaches an embodiment of claim 1, wherein the target cell or virus, if present in the sample, is allowed to bind to the magnetic microbead with high specificity to form the conjugate (p. 43, where immunomagnetic separation comprises using small super-paramagnetic beads coated with antibodies against surface antigens of cells; see Figure 1 and 2).

With regard to claim 18, Olsvik teaches an embodiment of claim 1, which further comprises washing the separated conjugate to remove the undesirable constituents before applying separated conjugate to a nucleic acid amplification system (p. 46, col. 1, where immunomagnetic separation concentrates bacteria into a suitable volume and removes PCR inhibtors, the cells are opened and the nucleic acid is available for PCR).

With regard to claim 22, Olsvik teaches an embodiment of claim 1, which is conducted in the absence of a precipitation or centrifugation procedure (Figure 2, where the cells bound to the particles are pulled to the side without precipitation or centrifugation).

With regard to claim 23, Olsvik teaches an embodiment of claim 1, which is conducted in the absence of a poisonous agent (p. 43-44, where the isolated bacterial fraction can be washed

before it is placed on a suitable growth medium, and therefore the method is conducted in the absence of a poisonous agent).

With regard to claim 27, Olsvik teaches an embodiment of claim 1, wherein the target cell is an epithelia cast-off cell or a bacteria cell isolated from saliva, urine and tissue culture (p. 43, where eukaryotic cells can be isolated from blood, or the technique can be applied to the detection of prokaryotic organisms such as bacteria and viruses).

With regard to claim 28, Olsvik teaches an embodiment of claim 1, wherein the nucleic acid amplification system is selected from the group consisting of polymerase chain reaction (PCR), ligase chain reaction (LCR), nucleic acid sequence-based amplification (NASBA), strand displacement amplification (SDA) and transcription-medicated amplification (TMA) (p. 46, col. 1, where immunomagnetic separation concentrates bacteria into a suitable volume and removes PCR inhibtors, the cells are opened and the nucleic acid is available for PCR).

With regard to claim 32, Olsvik teaches a process for amplifying a nucleic acid of a target cell or virus, which process comprises:

a) contacting a sample containing or suspected of containing a target cell or virus with a magnetic microbead (p. 43, where immunomagnetic separation comprises using small super-paramagnetic beads coated with antibodies against surface antigens of cells);

b) allowing said target cell or virus, if present in said sample, to bind to said magnetic microbead to form a conjugate between said target cell or virus and said magnetic microbead (p. 43, where immunomagnetic separation comprises using small super-paramagnetic beads coated with antibodies against surface antigens of cells; see Figure 1 and 2); and

c) separating said conjugate from other undesirable constituents via a magnetic force to isolate

said target cell or virus from said sample (see Figure 2, where the cells bound to the magnetic particles are removed using a magnet);

d) releasing a nucleic acid from said cell-microbead or virus-microbead conjugate to form a nucleic acid-microbead conjugate (p. 46, col. 1, where immunomagnetic separation concentrates bacteria into a suitable volume and removes PCR inhibtors, the cells are opened and the nucleic acid is available for PCR); and

d) applying said nucleic acid-microbead conjugate to a nucleic acid amplification system to amplify said nucleic acid from said target cell or virus (p. 46, col. 1, where immunomagnetic separation concentrates bacteria into a suitable volume and removes PCR inhibtors, the cells are opened and the nucleic acid is available for PCR; see also p. 46 and Figure 4).

With regard to claim 33, Olsvik teaches an embodiment of claim 32, which further comprises washing the nucleic acid-microbead conjugate to remove the undesirable constituents before applying the nucleic acid-microbead conjugate to a nucleic acid amplification system (p. 46, col. 1, where immunomagnetic separation concentrates bacteria into a suitable volume and removes PCR inhibtors, the cells are opened and the nucleic acid is available for PCR).

With regard to claim 34, Olsvik teaches an embodiment of claim 32, which further comprises separating nucleic acid-microbead conjugate from other undesirable constituents via a magnetic force before applying the nucleic acid-microbead conjugate to a nueleic acid amplification system (p. 46, col. 1, where immunomagnetic separation concentrates bacteria into a suitable volume and removes PCR inhibtors, the cells are opened and the nucleic acid is available for PCR).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lopez-Sabater et al. (Letters in Applied Microbiology, 1997, vol. 24, p. 101-104) as applied to claims 1, 4-7, 11-12, 14-18, 21-24 and 28-29 above and further in view of Miltenyi et al. (US Patent 5,691,208; November 1997). Lopez-Sabater teaches a method for the magnetic immunoseparation for detection of viral sequences by PCR (Abstract).

Lopez-Sabater teaches the limitations of claims 1, 4-7, 11-12, 14-18, 21-24 and 28-29 as recited in the 102 rejection stated above. However, Lopez-Sabater does not teach that the method is automated. Miltenyi teaches magnetic separators and devices for magnetic separation of cells (Abstract).

With regard to claim 19, Miltenyi teaches an embodiment of claim 1, which is automated (col. 12, lines 58-67 and col. 13, lines 1-17, where the separation system can be fully automated).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have applied the automated format of Miltenyi to the method of cell isolation and amplification to arrive at the claimed invention with a reasonable expectation for success. As taught by Miltenyi, "In the automated system, a computer controls the flow of fluids through the fluid circuitry and separation column, controls the magnetic field strength or

placement of the magnet and/or separation column to provide for the retention and release of the magnetically labeled target cells or analyte, and directs the final collection products into appropriate containers" (col. 12, lines 58-67). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have applied the automated format of Miltenyi to the method of cell isolation and amplification to arrive at the claimed invention with a reasonable expectation for success.

Claims 20 and 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olsvik et al. (Clinical Microbiology Reviews, 1994, vol. 7, no. 1, p. 43-54) as applied to claims 1-4, 6-10, 12-15, 17-18, 22-23, 27-28 and 32-34 above and further in view of Inuma et al. (Int. J. Cancer, 2000, vol. 89, p. 337-344). Olsvik teaches an overview of immunomagnetic separation using paramagnetic particles coated with antibodies for isolation of eukaryotic cells (p. 43, col. 1).

Olsvik teaches all of the limitations of claims 1-4, 6-10, 12-15, 17-18, 22-23, 27-28 and 32-34 as recited in the 102 rejection stated above. While Olsvik teaches that cells can be isolated from blood, regarding claim 26, Olsvik does not teach that the cells comprise leukocytes. Inuma teaches that leukocytes can be specifically targeted by magnetic beads comprising antibodies (p. 337, col. 2).

With regard to claim 26, Inuma teaches an embodiment of claim 1, wherein the target cell is a leukocyte isolated from whole blood, marrow or lympha (p. 337, col. 2, where 'anti-CD45 Mab-conjugated microbeads... bind to a common antiden of leukocytes').

Furthermore, regarding claims 20 and 26, Olsvik does not teach a specific time frame for practice of the invention. Inuma teaches a method that uses immunomagnetic separation to enrich for specific target cells followed by PCR amplification (Abstract).

With regard to claim 20, Inuma teaches an embodiment of claim 1, which is completed within a time ranging from about 0.5 minute to about 30 minutes (p. 338, col. 1, where the cells were resuspended with the microbeads and incubated for 15 minutes).

With regard to claim 25, Inuma teaches an embodiment of claim 1, wherein the sample volume ranges from about 5 uI to about 50 u1 (p. 338, col. 2, where the cells were separated using the MACS system and prepared for DNA extraction in 80µl of BSA-PBS).

Therefore, while Inuma does not teach the exact total time or total volumes required to practice the entire assay from start to finish, an ordinary practitioner would have recognized that the results optimizable variables of time, product amount and sample volume could be adjusted to maximize the desired results. As noted in *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the ? was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have applied the teachings of Inuma to the method of immunomagnetic separation taught by Olsvik to arrive at the claimed invention with a reasonable expectation for

success. As taught by Inuma, "prepared cells were resuspended in 80 µl of BSA-PBS mixed with 20 µl of CD45 microbeads for 15 min at 4°C and passed down the MACS column" (p. 338, col. 1). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have applied the teachings of Inuma to the method of immunomagnetic separation taught by Olsvik to arrive at the claimed invention with a reasonable expectation for success.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Hardingham et al. (Cancer Research, 1993, vol. 53, p. 3455-3458) teaches a general method for immunobead isolation of circulating tumor cells followed by PCR (Abstract).

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE K. MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stephanie K. Mummert
Patent Examiner
Art Unit 1637

/Stephanie K. Mummert/
Patent Examiner, Art Unit 1637